RISPERIDONE LONG-ACTING INJECTIONS: Successful Alternative Deltoid Muscle Injections for Refractory Schizophrenia

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ABSTRACT

Treatment-resistant paranoid schizophrenia is often addressed with long-term intramuscular preparations of conventional antipsychotics (haloperidol and fluphenazine), which can be associated with the development of painful, lumpy nodules at the injection site. In this article, we present a case example of a 58-year-old male patient with paranoid schizophrenia who was treated with risperidone long-acting injection given into the deltoid muscle instead of the US Food and Drug Administration (FDA)-approved gluteal muscle injection site. Use of this agent in the deltoid muscle facilitated healing of the numerous painful lumpy nodules associated with prior trials of conventional long-acting injections. In addition, the patient's psychiatric outcome was improved relative to what had been observed with the previous agents.

INTRODUCTION

Addressing long-term, treatment-resistant, paranoid schizophrenia with long-acting antipsychotic medication can be difficult due to side effects associated with the oil-based medium in which the medication is suspended. Specifically, this can lead to the development of painful, lumpy nodules at the injection site over time.[1] Given that problems with medication adherence are the most

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common factors associated with relapse in general, any improvements in reducing painful or problematic side effects are desirable. Risperidone long-acting is a water-based injection and may be better tolerated.[2]

Two recent studies support the use of the deltoid muscle as an alternative injection site for risperidone long-acting. In a large (170 patients) multicenter, open-label, single-dose, two-way, cross-over study, Thyssen, et al.,[3] studied the bioequivalence of risperidone long-acting injection administered into the deltoid versus gluteal muscle. In this study, no patient withdrew due to injection-site tolerability issues. Overall, 64 percent of patients experienced approximately one adverse event of swelling or redness (48% for gluteal injection and 49% for deltoid injection). However, of these reports, there were no nodule formations. Investigator-rated injection site reactions up to Day 15 revealed no difficulties at the injection sites. For the majority of patients, post-administration ratings of injection site pain by patients indicated minimal or no changes from 2 to 24 hours following injection.

In a similarly focused study, Ning, et al.,[4] reported the safety and tolerability of risperidone long-acting injection administered into the deltoid. This was an eight-week, multicenter, open-label, multidose study with 53 patients who required higher doses and who previously received risperidone long-acting gluteal injections. Patients received risperidone long-acting injection 37.5mg or 50mg every two weeks into the deltoid muscle. Doses were adjusted based on clinical need. Authors determined that both sites were safe and tolerable for risperidone long-acting injections. This study[4] had an 83-percent completion rate. No patients withdrew due to injection site tolerability issues. Investigator-rated mild injection site reactions were observed in 19 percent of patients after injection, but returned to normal prior to the next injection. Patients receiving the higher dose of medication reported higher pain than those receiving the lower dose. It is important to note that there was no evidence of nodule formation at the injection site.

Overall, Thyssen, et al.,[3] and Ning, et al.,[4] determined that risperidone long-acting injection was safe and well tolerated when administered as a single gluteal injection or as a single deltoid injection or multiple deltoid injections. This could be beneficial to patients who do not allow injections to be given at places other than the deltoid, due to paranoia or other psychiatric symptomatology.

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CASE REPORT

Mr. X, a 58-year-old, single, African-American man had been diagnosed with paranoid schizophrenia since 1973. He had a long history of multiple psychiatric hospitalizations and had been treatment refractory. The patient gave written informed consent to be interviewed for this publication. (The internal review board [IRB] of record was contacted prior to submission of this case report. A determination was obtained from that IRB that they do not consider case reports to be human research).

As a child, Mr. X was known to be a shy, introverted, nonassertive child with minimal social interactions with a comprehensive history of polysubstance and alcohol abuse. His first recorded psychotic episode was in 1973 when he was 23 years old. He fractured his leg after jumping from the second story of a building in response to his delusions. In 1985, he was arrested for breaking and entering, was found incompetent to stand trial, and the charges were dropped. He had been treated in an outpatient setting for the vast majority of his illness. Mr. X's last hospitalization, which lasted only a few days, was in 1987.

Mr. X received an adequate trial of several antipsychotics and mood stabilizers but was nonadherent and showed a definitive lack of improvement. He was given adequate trials of haloperidol, fluphenazine decanoate, thiothixene, and chlorpromazine. Combination therapies included haloperidol decanoate with lithium and valproate; lithium, carbamazapine, and fluphenazine; risperidone, halperidoldol, and valproate; olanzapine with valproate and thiothixene; and aripiprazole, valproate and haloperidol. Mr. X was either on haloperidol decanoate or fluphenazine decanoate at the maximum tolerated doses. He received fluphenazine decanoate from 1974 through 1980 and 1985 through 1987. From 1993 through 2007 he received haloperidol decanoate injections. He was given a trial of clozapine at 100mg but he developed excessive drowsiness and was nonadherent with the regular white blood cell (WBC) monitoring.

This patient's most persistent symptoms included paranoid delusions, grandiose ideation, blunted affect, inappropriate laughter and speech, preoccupation with self, irritability, loud verbal outbursts with obscenities, asocial behaviors, aggressiveness, impulsiveness, derailment, rarely assaultive behavior, and no insight into his illness. Mr. X had not had active homicidal or suicidal ideation. The presence of these symptoms after adequate trials with antipsychotics conforms to the definition for treatment refractory schizophrenia.[5]

Mr. X specifically remained inconsistent in taking oral antipsychotic medications at any time other than when he was in a day treatment program Monday through Friday. His inconsistent intake of medication during weekends, holidays, and evening hours created a conundrum in attempting to establish an adequate oral antipsychotic regimen. He therefore required an injectable antipsychotic treatment regimen for adequate treatment of his psychosis.

In the past, when Mr. X allowed injections in his gluteal muscles, he experienced excessive pain in his hips to the degree that he could not sit comfortably or sleep at night. Mr. X would accept his long-acting biweekly injections only in the left arm (deltoid) for at least seven years and would not allow the medication to be injected at any other site. As a result of the inability to rotate sites and the clinical necessity of injecting long-acting medications into the deltoid, he developed three egg-shaped, hard, painful, noninfected lumpy nodules in his left deltoid in 2007. These painful and hard lumpy nodules occupied approximately 75 percent of the deltoid.

Mr. X was informed by his psychiatrist and the treatment team about the FDA-approved gluteal site for risperidone long-acting injections. He did consent to a trial of an alternative deltoid site for risperidone long-acting injections starting on August, 7, 2007. These injections were administered deeply and slowly into the deltoid. The result of this intervention was a decrease in the size, pain, and density of these nodules considerably. In June of 2008, 10 months later, they occupied approximately 12 percent of the deltoid and were significantly less dense and tender. Qualitative improvements were also seen in treatment adherence with this patient. These improvements included impressions on the part of the involved treatment personnel that the patient was more open to clinical suggestions than previously and was less resistant to considering alternative courses of thought and action than had previously been observed. In some of these instances, the patient permitted changes in his treatment routine and alterations in daily activities, which were deemed to be positively correlated with clinical improvements, especially given that the narrow rigidity of his previous treatment response repertoire had closed off potential avenues for improvement.

The patient's medications were titrated up to 75mg of risperidone long-acting intramuscular injections every two weeks along with risperidone 8mg and aripiprazole 15mg orally each day. His irritability and agitation decreased to an extent where the patient was able to continue to live with his family and to independently commute using public transportation to and from his day treatment program Monday through Friday. He was also able to visit his internist regularly for management of hypertension. He had significantly fewer episodes of altercations with other patients, but continued to need redirection at times. He continued to experience an appreciable level of paranoia and still only allowed the risperidone long-acting injections to be administered by his psychiatrist.

DISCUSSION

Additional factors that contributed to this patient's clinical improvement include participation in a 25-hour-per-week day treatment program, residence with his caring brother and sister-in-law, family assistance in managing his finances, and medications for extrapyramidal side effects. It should be noted that this patient had in place the day treatment program and his family involvement when he was being treated with conventional antipsychotics in long-acting formulations. Treatment outcome under these conditions was inadequate in part, as indicated by the presence of episodes of irritability and aggression, psychological rigidity, and heightened paranoia. With the present treatment regimen, the patient had fewer verbal altercations with other patients, was more flexible in his behaviour, and allowed changes in his routines as a result of reduced paranoia.

Prior study results and the results of this case study support the safe and effective use of the deltoid muscle as an alternative injection site. As long-acting psychotropic medications become more available, bioequivalency studies on a variety of injection sites would be clinically useful.

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